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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,132	06/20/2003	Anthony P. Shuber	EXCT-31012/US-1/PRI	4962

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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/601,132	SHUBER, ANTHONY P.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8,11,14,19-21,24,28-30 and 35-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8,11,14,19-21,24,28-30 and 35-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/28/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/1/10 has been entered.

Claims 1, 4-8, 11, 14, 19-21, 24, 28-30, and 35-40 are pending and are currently under consideration.

Response to Arguments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-8, 11, 14, 19-21, 24, 28-30, and 35-37 remain rejected and newly added claims 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lapidus et al (US 6,143,529; 11/7/00) in view of Hromadnikova et al (BMC Pregnancy and Childbirth, 5/28/02, 2(4):1-5) for the reasons found in the Office Action of 10/24/08,

for the reasons stated in the Office Action of 6/29/09, and for the reasons set-forth below.

Lapidus et al teaches a method for identifying a patient as a candidate for additional colorectal cancer testing comprising the steps of: determining a quantitative amount of patient genomic DNA in a stool sample comprising shed cells and shed cellular debris, wherein the quantitative amount is determined by using quantitative PCR to measure an amount of nucleic acid fragments amplified from shed cells and shed cell debris, wherein a higher amount of amplifiable genomic DNA in a stool sample, as compared to a healthy individual, is highly predictive of colorectal cancer because patients with adenoma in the colon slough more cells than healthy individuals (see Example 2, Figure 1, and lines 42-46, in particular). Noting the 1kb ladder in Figure 1, Lapidus et al further teaches a quantitative amount of DNA in a sample would be obtained by detecting amplified nucleic acids less than 200bp in length (lines 43-47 of column 4 and Figure 1, in particular). Lapidus et al further teaches that patients identified as possibly having colon cancer by one method would also be subjected to other methods of testing for colon cancer (lines 8-10 of column 4, in particular). Such other methods comprise performing other diagnostic methods on the stool sample, LOH assay, detection of ras mutation, and colonoscopy (column 4, in particular).

Lapidus et al does not specifically describe the amounts of genomic DNA as "genome equivalents". However, this deficiency is made up in the teachings of Hromadnikova et al.

Hromadnikova et al teaches a quantitative PCR method of comparing amounts of DNA between samples comprising expressing amounts of DNA in terms of "genome equivalents" (page 2 right column, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to perform the methods of Lapidus et al by describing the amounts of DNA in terms of genomic equivalents because describing amounts of DNA in terms of genomic equivalents effectively normalizes data between multiple samples and assays. Further, one would have been motivated to perform said methods by detecting any amplifiable DNA because Lapidus et al teaches a high amount of amplifiable genomic DNA in a stool sample, as compared to a healthy individual, is highly predictive of colorectal cancer because patients with adenoma in the colon slough more cells than healthy individuals (see Example 2 and lines 42-46, in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for performing the methods of Lapidus et al by describing amounts of DNA in terms of genomic equivalents and detecting amplified DNA having lengths of 200bp or less because Hromadnikova et al teaches how to determine genome equivalents and because Lapidus et al teaches a high amount of amplifiable genomic DNA in a stool sample, as compared to a healthy individual, is highly predictive of colorectal cancer because patients with adenoma in the colon slough more cells than healthy individuals (see Example 2 and lines 42-46, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

When performing the combined method, amplified amounts of nucleic acid fragments above 10 genome equivalents would be identified as a candidate for additional testing because Lapidus et al teaches 200 pg as a "positive" result (see Example 2, in particular). *As evidenced by* Hu et al (BBRC, 2004, 313: 1058-1064), one human genomic equivalent would readily be found by the combined teachings to be 3 pg (see left column of 1059, in particular). Therefore, the 200 pg “positive” result of Lapidus et al is at least 10 genome equivalents for determining (i) whether a patient is a candidate for additional cancer testing, (ii) whether the patient has abnormal proliferating cancer cells, or (iii) whether the patient has colorectal cancer or precancer. Further, 500, 650, and 1000 genomic equivalents would be “positive” and indicate a patient is a candidate for additional cancer testing, that the patient has abnormal proliferating cancer cells, and that the patient has colorectal cancer or precancer.

In the Reply of 6/1/10, Applicant argues that Lapidus does not teach or suggest analysis of DNA fragments having length of less than 200 bp alone without measure of longer DNA in the same sample could be used as an indicator of colon cancer. Applicant further argues that Lapidus does not teach or suggest that measurement of the number of genome equivalents of DNA in fragments having lengths of less than 200 bp would sufficiently identify a patient as a candidate for additional colorectal cancer testing, especially in a stool sample. Applicant further argues that one of skill in the art would not be led to conduct tests on stool samples measuring only DNA having length below a minimum indicated size because Lapidus teaches determining the amount of DNA longer than 200 bp is required for identifying a patient as a candidate for additional

colorectal cancer testing based on a stool sample. Applicant argues the combined teachings do not teach or suggest every feature of the instant claims because Hromadnikova fails to teach or suggest determination of genome equivalents of nucleic acid fragments having length of 200 bp or less in a stool sample or that such determination could be used as a method of identifying a patient as a candidate for additional colorectal cancer testing.

The amendments to the claims and the argument found in the Reply of 6/1/10 have been carefully considered, but are not deemed persuasive. In regards to the argument that Lapidus does not teach or suggest analysis of DNA fragments having length of less than 200 bp alone without measure of longer DNA in the same sample could be used as an indicator of colon cancer, it is noted the claims are drawn to measuring DNA fragments that are amplification products having lengths of 200 bp or less. *The claims are not drawn to measuring genomic fragments of 200bp or less*. Further, Lapidus demonstrates analysis of DNA amplification fragments having length of less than 200 bp alone, without measure of longer DNA in the stool sample, as an indicator of colon cancer (see Example 2 and note the fragments of Figure 1, produced by the primers used in Example 2, are less than 200 bp).

In regards to the argument that Lapidus does not teach or suggest that measurement of the number of genome equivalents of DNA in fragments having lengths of less than 200 bp would sufficiently identify a patient as a candidate for additional colorectal cancer testing, Lapidus teaches a measurement of 200 pg of DNA fragments having lengths of less than 200 bp would sufficiently identify a patient as a candidate for

additional colorectal cancer testing (see Example 2 and lines 8-10 of column 4, in particular). *As evidenced by* Hu et al (BBRC, 2004, 313: 1058-1064), one human genomic equivalent would readily be found by the combined teachings to be 3 pg (see left column of 1059, in particular). Therefore, the 200 pg "positive" result of Lapidus et al is at least 10 genome equivalents for determining (i) whether a patient is a candidate for additional cancer testing, (ii) whether the patient has abnormal proliferating cancer cells, or (iii) whether the patient has colorectal cancer or precancer.

In regards to the argument that one of skill in the art would not be led to conduct tests on stool samples measuring only DNA having length below a minimum indicated size because Lapidus teaches determining the amount of DNA longer than 200 bp is required for identifying a patient as a candidate for additional colorectal cancer testing based on a stool sample, Lapidus teaches determining the amount of amplified DNA fragments less than 200 bp - without determining the amount of amplified DNA fragments longer than 200 bp – in order to identify a patient as a candidate for additional colorectal cancer testing based on a stool sample (see Figure 1, Example 2, and lines 8-10 of column 4, in particular).

In regards to the argument that Hromadnikova fails to teach or suggest determination of genome equivalents of nucleic acid fragments having length of 200 bp or less in a stool sample or that such determination could be used as a method of identifying a patient as a candidate for additional colorectal cancer testing, Lapidus teaches determination of genome equivalents of nucleic acid fragments having length of 200 bp or less in a stool sample or that such determination could be used as a method

of identifying a patient as a candidate for additional colorectal cancer testing (see Figure 1, Example 2, and lines 8-10 of column 4, in particular).

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Primary Examiner, Art Unit 1642